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Doran R. Pace, Patent Attorney

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 CFR 1.322
Docket No. FSU-100C2XC1
Patent No. 7,238,474

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	John L. Teem
Issued	:	July 3, 2007
Patent No.	:	7,238,474
For	:	Materials and Methods for Detecting Interaction of CFTR Polypeptides

Mail Stop Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION
UNDER 37 CFR 1.322 (OFFICE MISTAKE)

Sir:

A Certificate of Correction for the above-identified patent has been prepared and is attached hereto.

In the left-hand column below is the column and line number where errors occurred in the patent. In the right-hand column is the page and line number in the application where the correct information appears.

Patent Reads:	**Application Reads:**
Column 1, line 28:	Page 1, line 21:
"The ΔSF508"	--The ΔF508--
Column 18, line 4:	Page 27, line 2:
"identification"	--"Identification--
Column 31, line 20:	Page, claim 1, line 6:
"(NBD 1)"	--(NBD1)--

Column 31, line 21:	Page claim 1, line 7:
"NBD 1;"	--NBD1;--
Column 31, line 29:	Page, claim 1, line 12:
"NBD 1"	--NBD1--
Column 31, line 38:	Page, claim 1, line 18:
"NBD 1"	--NBD1--
Column 31, line 39:	Page, claim 1, line 18:
"NBD 1"	--NBD1--

A true and correct copy of pages 1 and 27 and claims pages of the specification, as filed which support Applicants' assertion of the errors on the part of the Patent Office, accompany this Certificate of Correction.

Approval of the Certificate of Correction is respectfully requested.

Respectfully submitted,

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DRP/dc/trt
Attachments: Copy of pages 1, 27 and claims pages of the specification;
Official Certificate of Correction

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,238,474

APPLICATION NO.: 10/089,875

DATED : July 3, 2007

INVENTOR : John L. Teem

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 1,
Line 28, "The ΔSF508" should read --The ΔF508--.

Column 18,
Line 4, "identification" should read --"Identification--

Column 31,
Line 20, "(NBD 1)" should read --(NBD1)--
Line 21, "NBD 1;" should read --NBD1;--
Line 29, "NBD 1" should read --NBD1--
Line 38, "NBD 1" should read --NBD1--
Line 39, "NBD 1" should read --NBD1--.

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DESCRIPTION

MATERIALS AND METHODS FOR DETECTING INTERACTION OF CFTR POLYPEPTIDES

Cross-Reference to Related Applications

This application claims the benefit of U.S. Provisional Application No. 60/157,996, filed October 6, 1999; U.S. Provisional Application No. 60/181,892, filed February 11, 2000; and U.S. Provisional Application No. 60/182,373, filed February 14, 2000.

Background of the Invention

Cystic fibrosis (CF) is the most common genetic disease of Caucasians in North America, occurring at a frequency of approximately 1 in 2500 births (Welsh *et al.*, 1995). The disease results from defective function of the gene encoding the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) protein in a variety of tissues, including the pancreas and the lung epithelium. Riordan *et al.* (1989), Rommens *et al.* (1989) and Kerem *et al.* (1989) describe the cloning and sequencing of the CFTR gene. U.S. Patent No. 5,543,399 to Riordan *et al.* discloses the purification of CFTR protein.

Normal CFTR protein is a membrane protein that functions as a cAMP-regulated chloride channel. The ΔF508 mutation in the CFTR gene, which is characterized by a deletion of the phenylalanine amino acid at position 508 of the CFTR protein, is the defect associated with most cases of CF. A CFTR protein having the ΔF508 mutation does not exit the ER and proceed on to the plasma membrane (Cheng *et al.*, 1990; Gregory *et al.*, 1991). It has been found that the ΔF508 mutation causes the temperature-sensitive misprocessing of the mutant protein that prevents the protein from exiting the ER (Denning *et al.*, 1992).

The absence of CFTR protein in the pancreatic duct results in the blockage of the duct by a thick mucus that prevents pancreatic enzymes from passing from the pancreas to the intestine. Without treatment, CF patients decline as a consequence of malnutrition associated with insufficient pancreatic function. However, pancreatic enzymes may be

Kerem, B.-S., J. M. Rommens, J.-A. Buchanan, D. Markiewicz, T. K. Cox, A. Chakravarti, M. Buchwald, L.-C. Tsui (1989) "Identification of the Cystic Fibrosis Gene: Genetic Analysis" *Science* 245:1073-1080.

Ma and Ptashne (1987) *Cell* 48:847-853.

Riordan, J. R., J. M. Rommens, B-S Kerem, N. Alon, R. Rozmahel, Z. Grzelczak, J. Zielenski, S. Lok, N. Plavsic, J-L Chou, M. L. Drumm, M. C. Iannuzzi, F. S. Collins, L.-C. Tsui (1989) "Identification of the Cystic Fibrosis Gene: Cloning and characterization of complementary DNA" *Science* 245:1066-1073.

Rommens, J. M., M. C. Iannuzzi, B-S Kerem, M. L. Drumm, G. Melmer, M. Dean, R. Rozmahel, J. L. Cole, D. Kennedy, N. Hidaka, M. Zsiga, M. Buchwald, J. R. Riordan, L.-C. Tsui, F. Collins (1989) "Identification of the Cystic Fibrosis gene: Chromosome walking and jumping" *Science* 245:1059-1065.

Sato, S., C. L. Ward, M. E. Krouse, J. J. Wine, R. R. Kopito (1996) "Glycerol reverses the misfolding phenotype of the most common cystic fibrosis mutation" *J Biol Chem* 271:635-638.

Sheppard, D. N., D. P. Rich, L. S. Ostedgaard, R. J. Gregory, A. E. Smith, M. J. Welsh. (1993) "Mutations in CFTR associated with mild-disease-form Cl- channels with altered pore properties" *Nature* 362:160-164.

Sheppard, D. N., M. R. Carson, L. S. Ostedgaard, G. M. Denning, M. J. Welsh (1994) "Expression of cystic fibrosis transmembrane conductance regulator in a model epithelium" *Am J Physiol* 266:L405-413.

Swick, A. G., M. Janicot, T. Cheneval-Kastelic, J. C. McLenithan, M. D. Lane (1992) "Promoter-cDNA-directed heterologous protein expression in Xenopus laevis oocytes" *Proc Natl Acad Sci USA* 89:1812-1816.

Teem, J. L., H. A. Berger, L. O. Sstedgaard, D. P. Rich, L-C Tsui, M. J. Welsh (1993) "Identificatioin of revertants for the cystic fibrosis ΔF508 mutation using STE6-CFTR chimeras in yeast" *Cell* 73:335-346.

Teem, J. L., M. Carson, M.J. Welsh (1996) "Mutation of R555 in CFTR-ΔF508 Enhances Function and Partially Corrects Defective Processing" *Receptors and Channels* 4:63-72.

Welsh, M. J., A. E. Smith, J. Zabner, D. P. Rich, S. M. Graham, R. J. Gregory, B. M. Pratt, R. A. Moscicki (1994) "Cystic fibrosis gene therapy using an adenovirus vector: in vivo safety and efficacy in nasal epithelium" *Hum Gene Ther* 5:209-219.

Welsh, M. J., A. E. Smith (1995) "Cystic fibrosis" *Sci Am* 273:52-59.

Allowed Claims

1 (amended by Examiner). A method for detecting or determining the interaction of a first CFTR polypeptide with a second CFTR polypeptide, said method comprising:

(a) providing a first polynucleotide encoding a fusion protein comprising all or a portion of a first CFTR polypeptide and a DNA binding domain of a transcriptional activator that can bind to a site on a detectable gene, wherein said first CFTR polypeptide comprises a first nucleotide binding domain (NBD1) of a CFTR polypeptide, or a functional fragment of said NBD1;

(b) providing a second polynucleotide encoding a fusion protein comprising all or a portion of a second CFTR polypeptide and a transcriptional activation domain of a transcriptional activator that can activate transcription of said detectable gene, wherein said second CFTR polypeptide comprises a first nucleotide binding domain (NBD1) of a CFTR polypeptide, or a functional fragment of said NBD1;

(c) incorporating said first and second polynucleotide into a host cell comprising said detectable gene wherein transcription of said detectable gene is under control of said transcriptional activator;

(d) expressing said polynucleotide encoding said first CFTR polypeptide and expressing said polynucleotide encoding said second CFTR polypeptide under conditions in which said detectable gene is expressed when said NBD1 of said first CFTR polypeptide and said NBD1 of said second CFTR polypeptide interact; and

(e) detecting transcription of said detectable gene or expression of the gene product of said detectable gene.

2. The method according to claim 1, wherein said host cell is a yeast cell.

3. The method according to claim 2, wherein said yeast cell is *Saccharomyces*.

4. The method according to claim 1, wherein the host cell is a mammalian cell.

5. The method according to claim 1, wherein said CFTR polypeptide is a mammalian